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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,677	BIRKELUND ET AL.	
	Examin r	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2002 and 04 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-17* is/are pending in the application.

4a) Of the above claim(s) *1-4,8,9,11,13 and 15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,7,10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-13 and 15-17* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' amendment D, of February 27, 2002 in Paper No. 20 is acknowledged. Claims number 1 and 8 were amended. New claim 17 was added.

2. It is noted that on the restriction of 9/27/2001 (paper # 18) there was a typographical error in regard to the group I. Claim 11 is part of group I because amended claim 11 is depending from claim 1. The examiner respectfully apologizes for the error.

Election/Restrictions

3. Applicants' election with traverse of February 27, 2002 in Paper No. 20 is acknowledged.

Applicants originally elected group I (claims 1-3, 6, 8 and 11) as drawn to antibodies against outer membrane of *Chlamydia pneumoniae.*

4. Applicants' substitute election with traverse of March 04, 2002 in Paper No. 21 is acknowledged. Applicants wished to elect group III (claims 5, 7, and 10,12) instead. Group III is directed to chlamydial proteins. Applicant elected SEQ ID NO 2 with traverse.

The traversal is on the ground(s) that the claimed chlamydial proteins were not known to the prior art, and define a unifying inventive concept justifying the joinder of groups I, II and IV to III has been noted.

This is not found persuasive because the four groups of inventions, are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature linking group I is considered to be antibodies and their methods of

use and detection.

The special technical feature linking group II is considered to be a nucleic acid.

The special technical feature linking group III is considered to be proteins, composition of said proteins and their method of use.

The special technical feature linking group IV is considered to be a method of immunization.

Accordingly, Groups I-IV are not so linked by the same or corresponding special technical feature as to form a single general inventive concept.

The lack of unity requirement is still deemed proper and is therefore made FINAL.

5. Claims 1-4, 8-9, 11, 13 and 15-17, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non elected groups I, II and IV.

6. Claims 1-13 and 15-17 are pending.

7. Currently claims 5, 7, 10 and 12 are under consideration.

Drawings

8. The drawings are objected to by the Draftsperson under 37 CFR 1.84 or 1.152. See attached form PTO 948.

Priority

9. Priority statement is missing from specification:

This application filed under former 37 CFR 1.62 lacks the necessary reference to the prior application. A statement reading "This is a U.S.C. 371 of Application No. PCT/DK98/00266, filed 6/19/1998 and claims priority to Danish application No. 0744/97, filed on 6/23/1997"."

should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of the parent nonprovisional application(s) should be included.

Information Disclosure Statement

10. Applicants' Information Disclosure Statement, paper # 6 is acknowledged. The listing of references in the specification (pages 33 and 34) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A (1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claim 5 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid shown in sequence ID # 2, which reads on a product of nature. The claims should be amended to indicate the hand of the inventor, e.g. by insertion of " isolated", as set forth in claim 5. See MPEP 2105.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex*

parte Dunki, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 5, 7, 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for the variants and subsequences claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims are directed to a protein derived from *Chlamydia pneumoniae* having amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof. The claims are broad and encompass any protein derived from Chlamydia *pneumoniae.* The specification indicates that "a variant will typically show a sequence similarity of preferably at least 50%, preferably at least 60%, preferably at least 70%, such as at least 80%, e.g. at least 90%, 95%, 98%." (see page 10, lines 10-14). The specification further indicates, " A subsequence will typically comprise at least 100 amino acids, preferably at least 80 amino acids, more preferably at least 70 amino acids, such as 50 amino acids. It might be as small as 10-50..." (see page 10 lines 29-34).

The specification does not provide any description of these variants and which positions in these variants can be altered without loss of protein activity or which position would render a non-functional protein. Furthermore, no examples of any of these variants are provided. No

information, beyond the characterization of SEQ ID NO: 2 have been provided by applicant, which would indicate possession of the claimed variants. No description has been provided by applicant of the variants encompassed by the claims. The specification has no disclosure of the function of all of the variants. Each variant and subsequences of the proteins claimed is a large variable genus, which can have a wide variety of functions. The art also teaches functionally unrelated molecules can be produced by these substitutions for example Van de Loo et al. (Proc. Natl. Acad. Sci 1995) teaches that polypeptides of approximately 67% homology to a desaturase from Arabidopsis were found to be hydrolases once tested for activity (see abstract). Similarly, Broun et al. (Science 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform an hydrolase into a desaturase (see abstract). Therefore, many functionally unrelated variants (polypeptides) are encompassed within the scope of the claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variants broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of prediction protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to

ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. Multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does **not** disclose the following:

- the general tolerance to modification and extent of such tolerance;
- specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which retain the biological activity if the intact protein; and
- the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicant have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed protein in manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and

undue. See Amgen Inc v. Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed.Cir.1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S.P.Q. 546(Bd. Pat. App. & Int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 5, 7, 10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite by reciting " A protein derived from *Chlamydia pneumoniae*". It should recite an isolated or purified protein.

It is not clear what applicants intended in recitation of " a similar biological function" in claim 5.

Recitation of the phrase " a variant or subsequence thereof" in claims 5, 7, 10 and 12 is indefinite. It is not clear what constitutes the meets and bounds of " a variant or subsequence thereof".

It is not clear what applicants intend in reciting " a mammal, such as a human" in claims 7, 10 and 12.

Claim 12 provides for the use of the protein, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to

encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 5, 7, 10, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting improper Markush group. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being " selected from the group comprising of A, B, and/or C." See exparte Markush, 1925 C.d. 126 (Comm'r Pat. 1925).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993). Prior art already made of record.

Claim 5 is drawn to a protein derived from *Chlamydia pneumoniae* having the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof having a sequence similarity of at least 50% and similar biological function.

Melgosa et al. teach a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract and

page 202). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa protein taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

15. Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 7 is drawn to a kit for diagnosis of infection of a mammal with *Chlamydia pneumoniae* comprising a protein with the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof. (The examiner views the claimed kit as a product or a composition comprising a protein of *Chlamydia pneumoniae*).

Melgosa et al. teach a product or a composition for diagnosis of infection of a mammal with *Chlamydia pneumoniae* comprising a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a composition of 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract) This composition was used for diagnosis of Chlamydia *pneumoniae* in rabbits (see page 201). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

16. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 10 is drawn to a composition for immunizing a mammal against *Chlamydia pneumoniae* comprising a protein with the amino acid sequence shown in SEQ ID NO: 2 or a variant or subsequence thereof.

Melgosa et al. teach a composition for immunizing a mammal against *Chlamydia pneumoniae* comprising a protein derived from *Chlamydia pneumoniae.* Melgosa et al. teach a composition of 98-kDa protein from outer membrane complex of *Chlamydia pneumoniae* (see abstract) This composition was used to immunize rabbits (see page 200). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i. e., that the product of prior art does not possess the same material structure and functional characteristics of the claimed product). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

17. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Melgosa et al. (FEMS Microbiology Letters Vol. 112, No. 2, pp. 199-204, September 1993).

Claim 12 is drawn to a method of use of a protein derived from *Chlamydia pneumoniae* shown in SEQ ID NO: 2 or a variant or subsequence thereof.

Melgosa et al. teach a method of use of a protein derived from *Chlamydia pneumoniae* (see page 200). SEQ ID NO: 2 or a variant of the claimed invention will be inherent in the 98-kDa-protein composition taught by Melgosa et al.

Since the office does not have the facilities for examining and comparing applicants' method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i. e., that the method of prior art does not possess the same method steps and functional characteristics of the claimed method). See In re Best, 562 F.2 d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Conclusion

18. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

May 25, 2002

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